WHAT IS CLAIMED IS:

1. A method of making water-soluble chitosan, said method comprising the steps of:

contacting water-insoluble chitosan with a basic solution for a first period of time;

rinsing the water-insoluble chitosan to remove any residual basic solution;

partially acetylating the water-insoluble chitosan in a reaction solution containing a phase transfer agent to form partially acetylated water-soluble chitosan;

dissolving the partially acetylated water-soluble chitosan in an aqueous solution containing a surfactant;

adjusting a pH of the aqueous solution to a pH of at least 7.0;

adding a water-miscible solvent into the aqueous solution having a pH of at least 7.0;

further adjusting the pH of the aqueous solution to a pH of at least 8.0 to cause precipitation of water-soluble chitosan having low endotoxin content;

separating the water-soluble chitosan having low endotoxin content from the aqueous solution; and

washing the water-soluble chitosan having low endotoxin content with the water-miscible solvent.

2. The method of Claim 1, wherein the basic solution comprises a 1M NaOH solution.

3. The method of Claim 1, wherein the first period of time ranges from about 1 hour to about 6 hours.

4. The method of Claim 3, wherein the first period of time ranges from about 2 hour to about 6 hours.

5. The method of Claim 1, wherein the aqueous solution having a pH of at least 7.0 comprises an aqueous solution having a pH of about 7.2.

6. The method of Claim 1, wherein the rinsing step comprises rinsing the water-insoluble chitosan with endotoxin-free water.

7. The method of Claim 1, wherein the reaction solution contains an acetylating agent selected from the group consisting of acetyl halides, acetic anhydride, and combinations thereof.

8. The method of Claim 7, wherein the acetylating agent comprises acetic anhydride.

9. The method of Claim 1, wherein the phase transfer agent comprises a quaternary ammonium salt, a quaternary phosphonium salt, a crown ether, or a pyridinium salt.

10. The method of Claim 1, wherein the phase transfer agent comprises a quaternary ammonium salt having a structure as shown in Equation I below:

$$[A]_w[B]_x[C]_y[D]_zN+Q \qquad (I)$$

wherein:

each of w, x, y, and z is independently an integer from 0 to 4 and w+x+y+z=4;

Q is a counter-ion selected from F^-, Cl^-, Br^-, I^-, CH_3COO^-, OH^-, HSO_4^-, NO_3^-, PF_6^-, BF_4^-, $HCOO^-$ and $H_2PO_4^-$; and

A, B, C and D are each independently selected from C_1-C_{18} alkyl; phenyl in which the phenyl ring is unsubstituted or substituted by C_1-C_8 alkyl, C_1-C_8 alkoxy, halo, hydroxy, phenoxy, nitro, carboxy, acetamido, or aryl; benzyl; and cycloalkyl have 5-6 ring member of heterocyclic ring system.

11. The method of Claim 10, wherein the phase transfer agent comprises tetrabutylammonium bromide.

12. The method of Claim 1, wherein the phase transfer agent comprises a quaternary phosphonium salts having a structure as shown in Equation II below:

$$[A]_w[B]_x[C]_y[D]_zP^+Q^- \qquad (II)$$

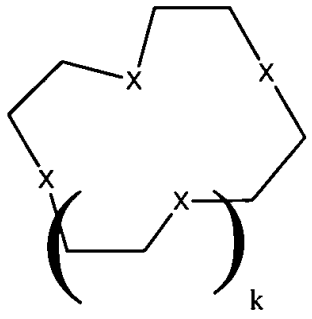
wherein:

each of w, x, y, and z is independently an integer from 0 to 4 and w+x+y+z=4;

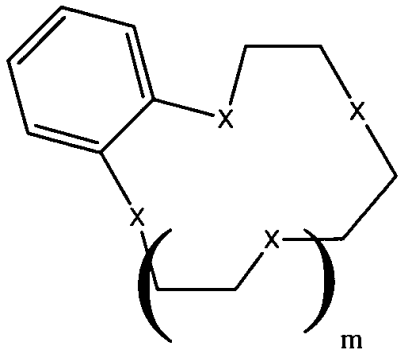
Q is a counter-ion selected from F^-, Cl^-, Br^-, I^-, CH_3COO^-, OH^-, HSO_4^-, NO_3^-, PF_6^-, BF_4^-, $HCOO^-$ and $H_2PO_4^-$; and

A, B, C and D are each independently selected from C_1-C_{18} alkyl; phenyl in which the phenyl ring is unsubstituted or substituted by C_1-C_8 alkyl, C_1-C_8 alkoxy, halo, hydroxy, phenoxy, nitro, carboxy, acetamido, or aryl; benzyl; and cycloalkyl have 5-6 ring member of heterocyclic ring system.

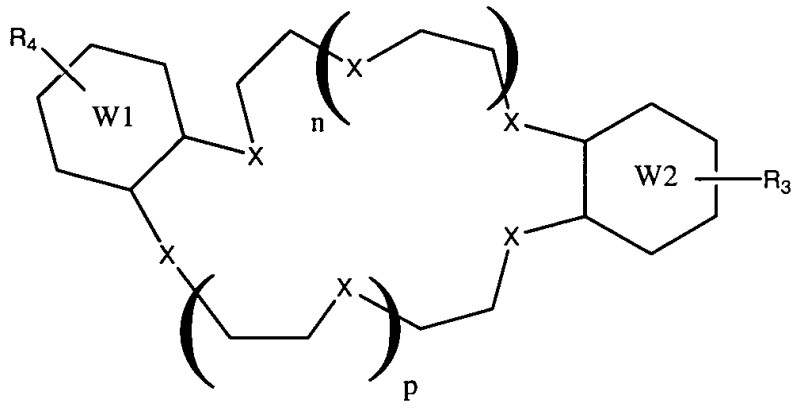
13. The method of Claim 1, wherein the phase transfer agent comprises at least one crown ether having a structure as shown in Equations IIIa-IIIc below:



IIIa



IIIb



IIIc

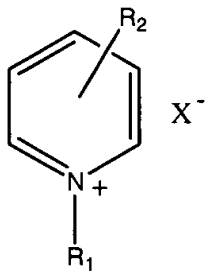
wherein each X independently represents O or S;

R_3 and R_4 each independently represent -H, C_1 to C_4 alkyl, or a halogen;

W1 and W2 each independently represent a cycloaliphatic ring or an aromatic ring; and

k, m, n and p each independently represent integers ranging from 1 to 3.

14. The method of Claim 1, wherein the phase transfer agent comprises at least one pyridinium salt having a structure as shown in Equation IV below:



IV

wherein:

R_1 represents C_1 to C_{18} alkyl, benzyl, or carboxymethyl;

R_2 represents C_1 to C_4 alkyl, chloro, fluoro, bromo, hydroxy, C_1 to C_4 alkoxyl or alkoxylcarbonyl; and

X represents a counterion of F, Cl, Br, I, or p-toluene sulfonate.

15. The method of Claim 1, wherein the partially acetylated water-soluble chitosan has a degree of N- acetylation of from about 24% to about 55%, and a degree of O- acetylation of from about 1% to about 60%.

16. The method of Claim 1, wherein the surfactant comprises polyoxyethylene sorbitan monolaurate.

17. The method of Claim 1, wherein the steps of adjusting the pH of the aqueous solution comprises adding a second basic solution to the aqueous solution.

18. The method of Claim 17, wherein the second basic solution comprises a 0.025 M NaOH solution.

19. The method of Claim 1, wherein the aqueous solution has a pH ranging from about 7.0 to about 7.4 after the first pH adjusting step.

20. The method of Claim 1, wherein the water-miscible solvent comprises isopropanol.

21. The method of Claim 1, wherein the water-soluble chitosan having low endotoxin content comprises less than about 100

equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

22. The method of Claim 1, wherein the water-soluble chitosan having low endotoxin content comprises less than about 50 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

23. The method of Claim 1, wherein the water-soluble chitosan having low endotoxin content comprises less than about 20 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

24. A water-soluble chitosan having low endotoxin content formed by the method of Claim 1, wherein the water-soluble chitosan having low endotoxin content comprises less than about 100 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

25. A water-soluble chitosan having low endotoxin content formed by the method of Claim 1, wherein the water-soluble chitosan having low endotoxin content comprises less than about 50 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

26. A water-soluble chitosan having low endotoxin content formed by the method of Claim 1, wherein the water-soluble chitosan having low endotoxin content comprises less than about 20 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

27. A method for making water-soluble chitosan, said method comprising the steps of:

contacting water-insoluble chitosan with a NaOH solution for a first period of time of greater than 1 hour;

partially acetylating the water-insoluble chitosan in a reaction solution containing a phase transfer agent to form partially acetylated water-soluble chitosan;

dissolving the partially acetylated water-soluble chitosan in an aqueous solution containing a surfactant and having a pH of from about 7.0 at about 7.4; and

adding a water-miscible solvent into the aqueous solution and further adjusting the pH of the aqueous solution to a pH of at least 8.0 to cause precipitation of water-soluble chitosan having low endotoxin content from the aqueous solution/water-miscible solvent mixture.

28. The method of Claim 27, wherein the method further comprises the steps of:

after the contacting step and prior to the acetylating step, rinsing the water-insoluble chitosan to remove any residual basic solution;

29. The method of Claim 27, wherein the method further comprises the steps of:

separating the water-soluble chitosan having low endotoxin content from the aqueous solution/water-miscible solvent mixture;

washing the water-soluble chitosan having low endotoxin content with the water-miscible solvent; and

drying the water-soluble chitosan having low endotoxin content.

30. The method of Claim 27, wherein the basic solution comprises a 1M NaOH solution.

31. The method of Claim 27, wherein the first period of time ranges from about 2 hours to about 6 hours.

32. The method of Claim 28, wherein the rinsing step comprises rinsing the water-insoluble chitosan with endotoxin-free water.

33. The method of Claim 27, wherein the reaction solution contains an acetylating agent selected from the group consisting of acetic anhydride.

34. The method of Claim 27, wherein the phase transfer agent comprises a quaternary ammonium salt, a quaternary phosphonium salt, a crown ether, or a pyridinium salt.

35. The method of Claim 27, wherein the phase transfer agent comprises a quaternary ammonium salt having a structure as shown in Equation I below:

$$[A]_w[B]_x[C]_y[D]_zN+Q \quad (I)$$

wherein:

each of w, x, y, and z is independently an integer from 0 to 4 and w+x+y+z=4;

Q is a counter-ion selected from F^-, Cl^-, Br^-, I^-, CH_3COO^-, OH^-, HSO_4^-, NO_3^-, PF_6^-, BF_4^-, $HCOO^-$ and $H_2PO_4^-$; and

A, B, C and D are each independently selected from C_1-C_{18} alkyl; phenyl in which the phenyl ring is unsubstituted or substituted by C_1-C_8 alkyl, C_1-C_8 alkoxy, halo, hydroxy, phenoxy, nitro, carboxy, acetamido, or aryl; benzyl; and cycloalkyl have 5-6 ring member of heterocyclic ring system.

36. The method of Claim 27, wherein the phase transfer agent comprises tetrabutylammonium bromide.

37. The method of Claim 27, wherein the partially acetylated water-soluble chitosan has a degree of N- acetylation of from about 24% to about 55%, and a degree of O- acetylation of from about 1% to about 60%.

38. The method of Claim 27, wherein the surfactant comprises polyoxyethylene sorbitan monolaurate.

39. The method of Claim 27, wherein the aqueous solution has a pH ranging from about 7.0 to about 7.2 prior to adding the water-miscible solvent.

40. The method of Claim 27, wherein the water-miscible solvent comprises isopropanol.

41. The method of Claim 27, wherein the water-soluble chitosan having low endotoxin content comprises less than about 100 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

42. The method of Claim 27, wherein the water-soluble chitosan having low endotoxin content comprises less than about 50 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

43. The method of Claim 27, wherein the water-soluble chitosan having low endotoxin content comprises less than about 20 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

44. A water-soluble chitosan having low endotoxin content formed by the method of Claim 27.

45. A partially acetylated water-soluble chitosan having a degree of N- acetylation of from about 24% to about 55%, and a degree of O-acetylation of from about 1% to about 66%, wherein the water-soluble chitosan comprises less than about 100 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

46. The water-soluble chitosan of Claim 45, wherein the water-soluble chitosan comprises less than about 50 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

47. The water-soluble chitosan of Claim 45, wherein the water-soluble chitosan comprises less than about 20 equivalent units (e.u.) of endotoxin per gram of dry water-soluble chitosan.

48. A pharmaceutically acceptable solution comprising the water-soluble chitosan of Claim 45 and at least one buffer material.

49. A pharmaceutically acceptable solution comprising the water-soluble chitosan of Claim 46 and at least one buffer material.

50. A pharmaceutically acceptable solution comprising the water-soluble chitosan of Claim 47 and at least one buffer material.